Mortality among Augmentation Mammoplasty Patients

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Much attention has focused on disease risks among women receiving silicone breast implants, but there has been little evaluation of their mortality experience. We undertook a retrospective cohort study of 13,488 women receiving cosmetic implants and 3,936 patients with other types of plastic surgery at 18 plastic surgery practices. After an average of 13 years of follow-up, deficits in overall mortality were found as compared with the general population (U.S. rates) for both implant [255 deaths; standardized mortality ratio (SMR) = 0.69, 95% confidence interval (CI) = 0.6–0.8] and comparison subjects (125 deaths; SMR = 0.58, 95% CI = 0.5–0.7). These findings indicate that patients seeking plastic surgery are in general healthier than their peers. Implant patients, however, experienced excess risks of death compared with the general population for brain cancer (SMR = 2.45) and suicide (SMR = 1.54). Internal analyses showed a higher overall mortality among the implant than among the comparison patients (relative risk = 1.27, 95% CI = 1.0–1.6). This overall excess reflected increases for respiratory tract (SMR = 3.03) and brain (SMR = 2.25) cancers and for suicide (SMR = 4.24). (Epidemiology 2001;12:321–326)

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The relation of breast implants to disease risk has been the topic of widespread attention and debate.[1,2] A number of epidemiologic studies have assessed relations with both cancer[3–6] and connective tissue disorders,[7–12] showing little evidence of adverse effects. Interpretation of results from these studies, however, has been complicated by a number of potential methodologic shortcomings, including small numbers of events, limited duration of follow-up, and the possibility of biased ascertainment of disease outcomes. Mortality among breast implant patients has not been extensively addressed, even though it is a well-defined outcome that should not be subject to possible biases resulting from events identified through patient contact.[13] Studies that have evaluated mortality among breast implant patients have limited their assessment to mortality from breast cancer.[6]

In this large follow-up study of women with augmentation mammoplasty, we evaluated mortality from various causes, comparing events with both an external standard (U.S. and regional mortality rates) and a group of comparison patients comprising women receiving other types of plastic surgery.

Subjects and Methods

This retrospective cohort study identified patients from 18 plastic surgery practices in six geographic areas (Atlanta, GA; Birmingham, AL; Charlotte, NC; Miami and Orlando, FL; and Washington, DC). We chose these practices because they had performed large numbers of cosmetic breast implant surgeries on a long-standing basis and were willing to give us unrestricted access to their records for purposes of subject identification and medical record abstraction. To improve opportunities for assessing long-term effects, we declared all female subjects who had a first bilateral augmentation mammoplasty at these practices during the period 1960–1988 to be eligible for the study. Because studying breast cancer incidence was a primary goal of the study, patients receiving a breast implant after a diagnosis of breast cancer were not included. A total of 13,488 subjects were identified for study. In addition, attempts were made, after identification of approximately every third to fourth eligible breast implant patient, depending on the practice, to identify a comparison patient in the same age range who had some other type of plastic surgery (not involving silicone) during the same time period in all but one practice (where permission for access to records of such patients was not obtained). We identified a total of 3,936 comparison subjects. Some subjects had multiple procedures. Prioritizing and categorizing operations showed that 20.5% had abdominoplasty or liposuction; 34.2% blepharoplasty or rhytidectomy (operations for the removal of wrinkles of the face

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and neck); 28.1% rhinoplasty, otoplasty, mentoplasty, or genioplasty (operations involving the nose, ear, and chin); and 17.2% another type of plastic surgery.

Trained medical records abstractors reviewed medical charts for eligibility. Using standardized software, data were directly entered into laptop computers. This information included patient identifiers as well as details on the types of surgery obtained (including implant type, manufacturer, and catalogue number), any noted complications, and other factors that might affect health status (for example, weight).

We determined vital status through a variety of tracing sources, including telephone directories, credit bureaus, postmasters, Motor Vehicle Administration records, and the National Death Index. A total of 10,782 (79.9%) of the implant patients and 3,219 (81.7%) of the comparison subjects were found to have objective evidence that they were still alive or to be identified as deceased (279 implant patients and 134 controls). Location rates varied by plastic surgery practice as well as by age, year of initial implant, and race, with the highest rates achieved for subjects who were older at their initial surgery, those with more recent dates of surgery, and white patients. It was not possible to verify reported deaths through acquisition of death certificate data for 7.5% of the implant and 4.5% of the comparison patients, and these subjects were treated as nonlocated patients. In addition, three augmentation and three comparison patients died within the first year of follow-up. For the remaining deceased patients (255 implant and 125 comparison patients), we determined causes of death through either death certificates or coded information available from the National Death Index-Plus system. Trained nosologists coded underlying causes of death using the *International Classification of Diseases* (9th revision) system.[14]

Statistical Methods

We accrued person-years beginning 1 year after the date of initial plastic surgery and continuing through the date of death or, for located subjects, through the end of 1997. We truncated follow-up time for nonlocated subjects on the date that the patient was last known to be alive. Few identifiers were available on these nonlocated subjects (including Social Security numbers), preventing assurance that their deaths would have been ascertained through National Death Index searches that extended through the end of 1997.

We calculated mortality rates, standardized to the 1970 U.S. population, for both implant and comparison subjects. In addition, we computed standardized mortality ratios (SMRs)[15] as the number of observed deaths divided by the expected number of events based on age, race, and calendar year-specific mortality rates for females from U.S. mortality data available for the period 1970–1995. The more stable U.S. rates were chosen over mortality rates for the states in which the practices were located, given that a large proportion of the women had moved over time; nonetheless, SMRs were essentially identical regardless of which rates were used.

We also conducted extensive internal analyses, based on the relative risk (RR), of mortality in the breast implant patients compared with that of the other plastic surgery patients.[15] We used Poisson regression methods, as implemented in the AMFIT module in the Epicure analysis package,[16] to calculate RRs, compute 95% confidence intervals (CIs), and adjust for potential confounding variables. For all analyses, the RR of implant status was adjusted for age at risk (5-year intervals through age 85), calendar year of follow-up (1960–1964, ..., 1990–1994, and 1995–1996), and race (white or black).

Results

The average age at entry into the cohort was 34.0 years among the implant patients *vs* 40.9 years among the comparison patients. This age discrepancy was primarily due to a large proportion of the comparison group comprising patients with abdominoplasties, operations that generally occur at older ages. The average time of cohort entry was more comparable between the two groups: 1982.8 for the implant patients *vs* 1984.1 for the comparison patients. The average years of follow-up for the two groups were 13.9 and 12.5 years, respectively.

The SMR for all causes of mortality among implant patients was 0.69 (95% CI = 0.6–0.8), whereas that among the comparison patients was 0.58 (95% CI = 0.5–0.7) (Table 1). Nearly every cause of death was decreased among implant patients as compared with the general population, with deficits observed for all malignancies (SMR = 0.79); endocrine, nutritional, metabolic, and immune diseases (SMR = 0.16); diseases of the circulatory system (SMR = 0.30); digestive system diseases (SMR = 0.45); and cirrhosis of the liver (SMR = 0.10). The deficit of all malignancies was mainly due to a decreased risk of mortality from breast (SMR = 0.55) and gynecologic cancers (0.52). Exceptions to reduced risks included deaths from brain cancer (SMR = 2.45), suicide (SMR = 1.54), pneumonia (SMR = 1.37), and emphysema (SMR = 1.36). It is of note, given previous suggestions linking implants to specific diseases, that there was no excess risk of death from hematopoietic malignancies (SMR = 0.71) or connective tissue disorders (SMR = 0.35, based on one death from lupus erythematosus) (data not shown). Hematopoietic malignancies among the implant patients caused four deaths from leukemia and five from non-Hodgkin's lymphoma (*vs* zero and two, respectively, in the comparison subjects). In addition, two control subjects died from myelofibrosis. No subjects died from multiple myeloma (totals of 1.6 deaths among implant patients and 1.2 among comparison patients were expected). Among the comparison patients, deficits were observed for all malignancies (0.67) and for diseases of the circulatory system (0.33).

Analyses based on internal comparison of the implant and comparison patients showed a slightly increased risk for all causes of death among the implant patients (RR = 1.27, 95% CI = 1.0–1.6). An eleva-

TABLE 1. Age-Standardized Death Rates (Per 100,000 Person Years) and Standardized Mortality Ratios (SMR) (Based on U.S. Mortality Rates, 1970 –1995) among Breast Implant and Comparison Patients, and Internally Derived Relative Risks (RR) of Mortality for Implant vs. Comparison Patients

	Implant Patients (PYs = 160,018)				Comparison Patients (PYs = 43,189)				Internal Comparisons	
	No. of Deaths*	Rate†	SMR	95% CI	No. of Deaths*	Rate†	SMR	95% CI	RR	95% CI
All causes of death	255	2.41	0.69	0.6–0.8	125	3.22	0.58	0.5–0.7	1.27	1.0–1.6
All malignancies	123	1.24	0.79	0.7–0.9	59	1.62	0.67	0.5–0.9	1.37	1.0–1.9
Digestive tract	17	0.12	0.73	0.5–1.2	17	0.27	1.09	0.7–1.7	0.68	0.3–1.5
Respiratory	32	0.38	0.94	0.7–1.3	10	0.19	0.44	0.2–0.8	3.03	1.4–6.5
Breast	23	0.11	0.55	0.4–0.8	8	0.08	0.41	0.2–0.8	1.14	0.5–2.8
Female genital	10	0.23	0.52	0.3–1.0	7	0.07	0.71	0.3–1.5	0.94	0.3–3.0
Bladder	1	0.01	1.26	0.2–8.9	2	0.05	3.10	0.8–12.4	0.41	0.0–5.9
Kidney	2	0.02	0.85	0.2–3.4	2	0.73	1.37	0.3–5.5	2.38	0.2–26.5
Brain	13	0.13	2.45	1.4–4.2	3	0.08	1.22	0.4–3.8	2.25	0.5–9.9
Hematopoietic	9	0.06	0.71	0.4–1.4	4	0.09	0.57	0.2–1.5	1.50	0.4–5.6
Benign neoplasms	4	0.01	2.49	0.9–6.6	1	0.01	1.26	0.2–8.9	1.13	0.1–11.4
Endocrine, metabolic diseases	2	0.02	0.16	0.0–0.6	3	0.74	0.38	0.1–1.2	0.78	0.1–7.0
Mental disorders	1	0.00	0.33	0.0–2.3	2	0.07	1.46	0.4–5.8	0.17	0.0–8.2
Nervous system, sensory organs	5	0.12	0.68	0.3–1.6	3	0.07	0.77	0.2–2.4	1.72	0.3–10.2
Circulatory system	26	0.35	0.30	0.2–0.4	22	0.25	0.33	0.2–0.5	0.87	0.5–1.6
Arteriosclerosis, CHD	13	0.21	0.30	0.2–0.5	9	0.12	0.24	0.1–0.5	1.43	0.6–3.5
Vascular lesions	4	0.02	0.25	0.1–0.7	5	0.05	0.46	0.2–1.1	0.49	0.1–2.1
Respiratory disease	21	0.34	1.02	0.7–1.6	13	0.22	0.82	0.5–1.4	1.56	0.7–3.3
Pneumonia	8	0.05	1.37	0.7–2.7	5	0.07	1.30	0.5–3.1	1.46	0.4–5.2
Emphysema	3	0.03	1.36	0.4–4.2	1	0.03	0.49	0.1–3.5	3.21	0.3–35.5
Digestive system diseases	8	0.04	0.45	0.2–0.9	6	0.06	0.64	0.3–1.4	0.92	0.3–3.0
Cirrhosis of liver	1	0.00	0.10	0.0–0.7	3	0.03	0.66	0.2–2.1	0.35	0.0–3.4
Genitourinary diseases	3	0.01	0.79	0.3–2.4	1	0.01	0.38	0.1–2.7	0.79	0.1–9.7
Senility and ill defined	2	0.01	0.42	0.1–1.7	2	0.02	1.05	0.3–4.2	0.26	0.0–2.1
All external causes	51	0.16	1.18	0.9–1.6	12	0.13	0.97	0.5–1.7	1.43	0.7–2.8
Accidents	23	0.07	0.95	0.6–1.4	8	0.08	1.06	0.5–2.1	0.90	0.4–2.2
Suicide	19	0.07	1.54	1.0–2.4	2	0.02	0.61	0.2–2.4	4.24	0.9–19.2

CHD, coronary heart disease.
* Shown are causes of death with at least two deaths in either of the study groups.
† Age-standardized to the 1970 U.S. population.

tion was observed for all malignancies (RR = 1.37, 95% CI = 1.0–1.9), with this largely driven by an excess risk for respiratory tract cancer (RR = 3.03, 95% CI = 1.4–6.5). Excesses were seen for brain cancer (RR = 2.25, 95% CI = 0.5–9.9) and suicide (RR = 4.24, 95% CI = 0.9–19.2). Mortality from diseases of the circulatory system was similar in the implant and comparison subjects (RR = 0.87, 95% CI = 0.5–1.6).

The SMRs among the implant patients for most causes of death did not vary much by calendar year of implantation, age at initial breast implantation, or interval since implantation (Table 2). An exception was an excess risk of death from external causes among subjects who had their operations at 40 years of age or later. This excess derived from an increased risk of suicide among subjects with older ages at implantation (SMR = 3.89, 95% CI = 2.0–7.5). More than twofold elevations in suicide deaths were also observed among subjects with 10 or more years of follow-up. Although the majority of implant patients demonstrated a substantially reduced risk of malignancy, subjects with 15 or more years of follow-up were no longer at reduced risk. This trend reflected the absence of any reduction in risk of respiratory tract cancer (SMR = 1.07) among the subjects with extended follow-up. The risk of nonmalignant respiratory disease was highest, and no longer reduced, among subjects who had their operations at older ages (35+ years) or who had longer intervals (10+ years) between implantation and development of disease.

We examined the risk of death among implant *vs* comparison patients according to these same time-related factors (Table 3). There was little variation in risk from all causes or individual causes of mortality by most of these parameters. Subjects with older ages at surgery did show an excess risk of malignancy (RR = 1.47, 95% CI = 1.0–2.2). Twenty-five augmentation patients who had surgery at older ages died of respiratory tract cancer, resulting in a RR of 2.92 (95% CI = 1.4–6.3). Subjects with extended follow-up (15+ years) also showed some elevation in the risk of death from all causes and from malignancies. This latter effect primarily reflected an elevation in mortality from respiratory tract cancer (RR = 2.93, 95% CI = 0.8–10.3).

A total of 49.7% of the implant patients received silicone gel implants, 34.1% double-lumen implants, 12.2% saline-filled implants, 0.1% other types of implants, and 3.8% unspecified types of implants. The SMRs for all causes did not vary substantially by the type of implants: 0.73 for silicone gel implants, 0.65 for double-lumen implants, 0.65 for saline-filled implants, and 0.55 for unspecified types of implants. Although there was little variation in the risk of individual causes by type of implant, the SMR for suicides was elevated for

TABLE 2. Standardized Mortality Ratios (SMR) for Selected Causes of Death among Breast Implant Patients: Comparisons Based on U.S. Mortality Rates, 1970–1995

	All Causes		Malignancies		Circulatory System		Respiratory Disease		All External Causes	
	SMR	No. of Deaths*	SMR	No. of Deaths*	SMR	No. of Deaths*	SMR	No. of Deaths*	SMR	No. of Deaths*
Calendar year										
<1975	0.61	39	0.67	18	0.43	7	0.79	3	1.16	7
1975–1979	0.82	119	1.03	63	0.28	10	1.33	11	1.27	19
1980–1984	0.59	66	0.68	32	0.24	6	0.84	5	1.08	15
1985+	0.60	31	0.48	10	0.30	3	0.82	2	1.23	10
Age at surgery, years										
<30	0.66	39	0.66	13	0.11	1	0.92	2	0.98	15
30–34	0.63	46	0.72	22	0.29	4	0.00	0	1.12	13
35–39	0.66	50	0.76	26	0.36	6	1.08	4	0.99	8
40+	0.73	120	0.87	62	0.32	15	1.30	15	1.87	15
Interval since surgery, years										
<5	0.63	35	0.65	13	0.48	5	0.46	1	1.09	13
5–9	0.44	42	0.46	18	0.15	3	0.45	2	0.86	12
10–14	0.76	80	0.74	34	0.24	6	1.19	7	1.39	14
15+	0.84	98	1.13	58	0.38	12	1.38	11	1.71	12

* Number of deaths among augmentation patients.

patients with silicone gel implants (SMR = 1.81, 95% CI = 1.0–3.2).

To address concerns that truncating person-years of follow-up at the time of last known vital status for the nonlocated subjects may have affected the estimation of risk, we performed selected analyses with different assumptions regarding losses to follow-up. Among the nonlocated patients, 50.8% of the implant and 55.8% of the comparison patients had sufficient identifiers (name, date of birth, and Social Security number) that their deaths would have almost certainly been identified through linkage with the National Death Index. As expected, the assumption that all of these subjects were alive at the end of the study further reduced the mortality risks for both implant and comparison patients as contrasted with the general population (respective SMRs of 0.62 and 0.53). If all subjects lost to follow-up were assumed alive at the end of the study period, the respective SMRs were 0.59 and 0.53, respectively. The RRs under different assumptions were essentially unchanged from those previously derived. The RR assuming that only subjects with sufficient identifiers were alive at the end of the study period was 1.28 (95% CI = 1.0–1.6), whereas the RR based on the assumption that all nonlocated subjects had survived until the end of the follow-up period was 1.27 (95% CI = 1.0–1.6).

Discussion

Although the long-term effects of breast implants have received much attention, few previous studies have addressed the issue of mortality among these patients. A limitation of a mortality analysis is that diseases with a poor prognosis will be overrepresented as compared with an incidence analysis. In addition, some causes of death may be erroneously assigned on death certificates, although it is doubtful that this miscoding would occur differently for breast implant *vs* other patients. The strength of such an analysis is that deaths can be readily and completely ascertained for cohort members through linkage against national registries. This information reduces questions regarding potential effects of selection

TABLE 3. Relative Risks (RR) of Deaths for Selected Causes of Death among Breast Implant Patients: Comparisons Based on Other Plastic Surgery Patients

	All Causes		Malignancies		Circulatory System		Respiratory Disease		All External Causes	
	RR	No. of Deaths*	RR	No. of Deaths*	RR	No. of Deaths*	RR	No. of Deaths*	RR	No. of Deaths*
Calendar year										
<1975	1.63	19	1.21	11	1.87	3	4.45	1	∞	0
1975–1979	1.35	38	1.41	18	0.86	7	0.82	7	4.42	1
1980–1984	1.09	43	1.99	14	0.42	12	5.53	2	0.60	8
1985+	0.91	25	0.51	16	∞	0	1.56	3	1.39	3
Age at surgery, years										
<30	0.71	7	0.39	4	0.14	1	∞	0	2.31	1
30–34	1.36	4	2.27	1	∞	0	0.00	0	0.80	2
35–39	1.37	6	1.43	3	∞	0	0.48	1	0.75	2
40+	1.32	108	1.47	51	0.81	21	1.73	12	1.74	7
Interval since surgery, years										
<5	1.58	17	1.38	9	1.48	4	1.57	1	2.45	2
5–9	0.71	34	0.73	15	1.31	3	0.87	4	0.63	6
10–14	1.19	40	1.32	14	0.32	13	2.48	3	1.16	4
15+	1.57	34	1.49	21	4.06	2	1.45	5	∞	0

* Number of deaths among comparison patients; see Table 2 for numbers of deaths among augmentation patients.

and recall biases that often arise within the context of studies of disease incidence in which outcome information is based on patient contact.

Although breast implant patients had an increased risk of death compared with other patients undergoing plastic surgery, both groups of patients actually had a lower mortality than the general population. This finding supports the notion that patients who choose to undergo plastic surgery are self-selected in terms of generally being healthy, a situation that is well recognized in mortality studies of occupationally exposed cohorts.[17,18]

Previous mortality studies among breast implant patients have primarily focused on breast cancer. Breast cancer mortality has been of interest given that implants have been shown to interfere with mammographic visualization of lesions,[19–22] possibly leading to a shift toward later detection of breast cancers. Although a few clinical studies have suggested that patients with breast implants who develop breast cancer have unusually advanced cancers,[23] epidemiologic studies that have examined stage at diagnosis,[24,25] survival,[25,26] or mortality experience from breast cancer[6] have not confirmed substantial adverse effects. Thus, in line with our results, one record linkage study in Sweden found a 50% reduction in breast cancer mortality among breast implant patients as compared with the general population.[6]

Although most causes of death were reduced among the implant patients as compared with the general population, a few were elevated, most notably deaths from brain cancer, pneumonia, emphysema, and suicide. Notable was the absence of any excess of deaths from various diseases suggested as being related to exposure to silicone, including selected cancers (such as sarcoma, multiple myeloma, and other hematopoietic malignancies)[1] and a variety of connective tissue disorders (such as scleroderma, Sjögren's disease, and lupus erythematosus).[2] These diseases are rare in the general population and are not usually fatal in the short term, so the absence of any excess mortality does not eliminate concerns about a possible increase in incidence. Studies to date, however, have not generally confirmed an excess incidence of connective tissue diseases.[7–11]

As with most other healthy cohorts, the deficit from all causes of death among the implant patients as compared with the general population mainly reflected a lower risk of death from all malignancies and deaths of the circulatory system. The mortality from circulatory disease remained low during all follow-up periods, but the rate of malignancies was similar to that in the general population after 15 or more years of follow-up. This similarity was primarily due to the increasing risk of respiratory tract cancer among the augmentation patients after extended follow-up.

It has previously been demonstrated that patients with breast implants differ from the general population, tending more often to bear their children at young ages, terminate pregnancies, use oral contraceptives, have multiple lifetime sexual partners, use hair dyes, and drink alcoholic beverages.[27] Although we were not able to adjust for these variables because questionnaire data were not available for deceased subjects, we previously have demonstrated that use of plastic surgery controls eliminates many of these differences.[28] Thus, it was of interest that when we examined internal comparisons a slight excess risk of death among implant patients persisted, mainly reflecting their higher risks for malignancies (primarily respiratory tract cancers) and all external causes, particularly suicide.

The excess mortality from respiratory tract cancers was unexpected. This finding may be due to a higher rate of cigarette smoking in breast implant as compared with the patients with other types of plastic surgery, particularly given that we also observed that implant patients have a higher rate of nonmalignant respiratory diseases. Cancer of several other smoking-related sites (for example, bladder cancer) was not excessive among the implant patients, and our analyses among surviving patients did not discern any substantial difference in smoking patterns, including years smoked.[26] This result may have been due to imprecise or incomplete smoking information, particularly for deceased subjects. On the other hand, a number of case reports have noted pulmonary complications after exposure to silicone, including pneumonitis presumed to be due to a silicone embolus.[29–31]

The only other major causes of death that were excessive among breast implant as compared with the other patients were brain cancers and suicides, with these associated, respectively, with twofold and fourfold excess risks. Given the limited numbers of deaths from either of these causes, the possibility that these were chance findings cannot be ruled out. Brain cancers have not previously been documented as a site at altered risk among implant patients, although excesses, had they existed, would have been difficult to detect in most of the previous smaller investigations.[1] Suicide attempts have been correlated with a number of characteristics,[32] including marital difficulties, depression, and emotional disorders, all of which have been noted among patients with breast implants.[33] Low self-esteem, which has been commonly noted among breast implant patients,[34] may have also contributed to the suicide excess, especially if the implants did not achieve the desired effect or if problems with the implants were encountered. It is also possible, however, that the implants may have been more directly involved, especially given that implant patients have previously been found to manifest neurologic alterations[35,36] and in this study had elevated risks of brain cancers. The relation of breast implants to neurologic diseases, however, remains controversial, with some studies failing to find any relation.[37,38]

In summary, the findings of this study showed that women with breast implants have slightly higher mortality risks than patients with other types of plastic surgery and that both groups fare substantially better than the general population. This latter observation is in line with the notion that both groups of patients, similar to others undergoing elective surgery, are in general healthier than their peers. In determining the extent to which breast implants might affect mortality, it appears that patients with other types of plastic surgery are a more appropriate comparison group than the general population. In internal comparisons, the only causes of mortality that appeared to differ to any substantial effect were malignant and nonmalignant diseases of the respiratory tract, brain cancer, and suicide.

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